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EXAMINER	
FISHER, ABIGAIL L	

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1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,990	SCHACHT ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner for your application in the USPTO has changed. Examiner Abigail Fisher can be reached at 571-270-3502.

Receipt of Amendments/Remarks filed on July 29 2008 is acknowledged. Claim 7 was/stands cancelled. Claims 1-6 and 8-18 are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Terminal Disclaimer

The terminal disclaimer filed on July 29 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application No. 10623864 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Abstract

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because the abstract is limited to a single paragraph. Correction is required. See MPEP § 608.01(b).

Specification

The disclosure is objected to because of the following informalities: oxybutynin (as oxybutynine) is spelled incorrectly on page 6 line 17.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The specification, while being enabling for the treatment of Parkinson's disease with rotigotine, urinary incontinence with oxybutynin and fesoterodine and pain with fentanyl, does not reasonably provide enablement for the treatment of all diseases with all amine functional drugs. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Formal, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re

Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, relative skill level, and breadth of the claims

The instant invention is directed to a method for the treatment of a patient suffering from a disease treatable with an amine functional drug.

The complex nature of the claims is greatly exacerbated by the breath of the claims. The claims encompass any disease with any amine functional drug.

The relative skill of those in the art is high, that of an MD or PHD.

The state and predictability of the art

The state of the art recognizes as well as the instant specification recognizes that specific drugs can treat specific diseases. It is recognized that Parkinson's disease can be treated with rotigotine, urinary incontinence can be treated with oxybutynin and fesoterodine and pain can be treated with fentanyl.

The lack of significant guidance from the specification or the prior art with regard to treating any disease utilizing amine functional drug makes practicing the scope of the invention unpredictable. The scope of the instant claims includes all diseases yet to be discovered that can be treated with amine functional drugs as well as yet to be discovered anime functional drugs.

The amount of direction or guidance provided and the presence or absence of working examples

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The specification provides no direction or guidance for how to treat any disease with any amine functional drug. Due to the vastness of compounds classified as amine functional drugs, one of ordinary skill would undergo undue experimentation in deducing which drugs can actually treat which diseases within applicant's scope. Specifically, one of ordinary skill in the art would have to determine which drugs are amine functional drugs and then test each drug in every known disease in order to determine what diseases can be treated with these drugs. The drug discovery process is difficult due to the complex nature of diseases. Therefore, one of ordinary skill in the art has no assurances of success of finding any other diseases that can be treated with amine functional drugs.

The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to treat any disease as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claims 1-5, 8, and 10-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification

in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as oxybutynin, rotigotine, fesoterodine, fentanyl, aminotetralin, and silica which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim(s) 1-5, 8, and 10-18 is(are) directed to encompass any amine functional drug, which only corresponds in some undefined way to specifically instantly disclosed chemicals. Claim 10 additionally recites that the matrix is free of particles that can absorb salts of the amine functional drug. None of these amine functional drugs or particles that can absorb salts of the amine functional drug meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. Applicants have provided no definition as to what constitutes an amine functional drug excpet indicating four specific drugs that are considered amine functional drugs. Applicants have only indicated particles that can absorb salts of the amine functional drug are silica. Additionally, claims 3 and 4 recite that the amine functional drug has an octanol/water partitioning coefficient (log p) $\geq$ 2.8 at pH 7.4 and a pKa of 7.4 to 8.4. The instant application only claims one specific drug and that is oxybutynin, however as evidenced by Quan et al. (US Patent No. 5834010, cited on PTO Form 1449), Oxybutynin has a pKa of 10.3 (example 1), which is outside of the claimed range, therefore this compound would not meet the limitations of this claim. The specification

does not specifically point out any drug that would meet the limitation of instant claims 3 or 4. The specification provides insufficient written description to support the genus encompassed by the claim. **Note: MPEP 2163.**

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, (Fed. Cir. 1991), makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), further supports this by stating that:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed amine functional drugs or particles**,** regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Circ. 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, (Fed. Cir. 1991). In Fiddes v. Baird, 30 USPQ2d 1481, 1483, (Bd. Pat. App. & Int. 1993), claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 (Fed. Cir. 1997) held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir.

> 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Furthermore, to the extent that a functional description can meet the requirement for an adequate written description, it can do so only in accordance with PTO guidelines stating that the requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics," including "functional characteristics when coupled with a known or disclosed correlation between function and structure." Univ. of Rochester v. G.D. Searle, 68 USPQ2d 1424, 1432 (DC WNY 2003).

Therefore, only the above chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 10-11 and 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. (US Patent No. 5932240) in view of Muller et al. (WO 99/49852, cited on PTO Form 1449) as evidenced by Nugroho et al. (Pharmaceutical Research 2004).

Applicant Claims

Applicant claims a transdermal delivery system comprising a backing layer, a self adhesive matrix containing an amine-functional drug and a protective foil or sheet to be removed prior to use wherein the self-adhesive matrix comprises a sold or semisolid

semi-permeable polymer wherein an amine functional drug in its free base form is incorporated which comprises within the matrix 10^3 to 10^9 microreservoirs per cm^2 of the surface of the matrix, said microreservoirs containing the amine functional drug which is permeable to the free base of the amine functional drug which is substantially impermeable to the protonated form of the amine functional drug and wherein the microreservoirs have a maximum diameter that is less than the thickness of the matrix and is not greater than 34 micrometers and wherein the backing layer is inter to the components of the matrix.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

D'Angelo et al. (US Patent 5,932,240) teach multidose transdermal drug delivery system comprising a laminate composite with a plurality of compartments, wherein each compartment is a reservoir for a unit dose of a drug active to be transdermally administered, wherein said unit doses being in the form of a multiphase composition of microspheres wherein an internal phase comprises the drug actives and adjuvants, and said internal phase is surrounded by an outer phase of film-forming polysaccharides engrafted with transdermal promoters, said microspheres being distributed through a diffusible matrix of said composition (abstract and reference claim 1). The patch assembly consists of a base in which the steady state dosage is contained as needed by the patient and individual medicament reservoirs which may be activated by either a "tear-and-release" or "pull-and-release" mechanism (i.e. backing layer; col. 2, lines 56-61). The reservoirs contain medicament which can be the same as contained in the base or various unit dosages of the base (col. 2, lines 61-67). D'Angelo et al. teach that

various drugs can be delivered in unit doses, including antiparkisonism drugs (col.1, lines 57 to col. 2, line 21; col. 2, line 67 to col. 3, line 8). D'Angelo et al. teach a multidose transdermal drug delivery system comprising a laminate composite of a drug-permeable membrane to be placed in contact with a patient's skin; a transfer gel layer disposed on the membrane; a permeable membrane disposed on the transfer gel layer; overlaid impervious drug enclosure means for receiving and protectively enclosing a drug active to be transdermally administered; wherein the drug enclosure means and the permeable membrane defining a plurality of compartments there between defining reservoirs for respective unit doses of the drug active; and individual activation means for releasing unit doses of the drug active form respective ones of the compartments for contacting with the patient's skin (col. 3, lines 9-23). D'Angelo et al. teach reservoirs comprising microencapsulations of the drug active, wherein the drug active may be insulin encapsulated into capsules of substantially 1 to 150 microns diameter, the microencapsulations are formed of a layer of polymer encapsulating the drug active, the polymer layer having drug-penetration moieties engrafted thereon (col. 3, lines 51-57). D'Angelo et al. disclose that laminate composite forming the reservoirs for the drug actives and associated vehicles may be formed from flexible or rigid materials, including regenerated cellulose (cellophane), ABS polymer/cellulose acetate (col. 4, lines 44-56). D'Angelo et al. teach Cotran 9872 acrylate adhesive for adhering the patch to the skin (= **self-adhesive layer**; col. 7, lines 2-9).). D'Angelo et al. teach that useful dimensions for the patch are approximately one inch by two inches and up to about one quarter to half inch in thickness (col. 4, lines 61-63), while the size of each reservoir is determined

by the volume of the unit dose to be administered (col. 4, lines 63-67). D'Angelo et al. teach that the drugs and their adjuvants are dissolved, suspended, absorbed or contained in matrices or solutions, wherein useful matrices are gels of bipolymers such as alginates, gelatins, chitin, and **PVP** (col. 5, lines 2-3). The size of the microcapsules varies between 1 and 150 microns depending on the desired concentrations of the drugs to be administered (column 6, lines 19-21).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

Although D'Angelo et al. al. teach that transdermal drug delivery systems wherein various drugs, such as antiparkinsonism drugs may be included in the microreservoirs, and acrylate adhesive for adhering the patch to the skin, this reference does not teach the specific instantly claimed aminotetralin compound or silicone pressure adhesive. However, this deficiency is cured by Muller et al.

Muller et al. (where US Patent No. 6884434 is serving as the English Language equivalent of WO 99/49852) is directed to a transdermal therapeutic system which contains a D2 agonist. The device is utilized for the treatment of Parkinson's syndrome (column 1, lines 9-10). The matrix systems for drug delivery in their simplest forms consists of a backing layer, an active substance containing self-adhesive matrix and a protective film to be removed prior to use (column 2, lines 51-56). The adhesive system are either acrylate-based or silicone-based (column 2, lines 36-37). Silicone adhesives are in most cases polydimethylsiloxanes. However other organic residues may in principle be present instead of the methyl groups. The silicone adhesives are available as one component adhesives in two variants as so-called amine-resistant and as non-

amine-resistant adhesives. Due to the basic nature of rotigotine (5,6,7,8-tetrahydro-6-[propyl-2[-(20thienyl)ethyl]amino-1-naphthalenol), silicone adhesives that are amine-resistant are used (column 3, lines 1-10). The adhesive's dissolving capacity of the active substance is an important parameter for the development of matrix systems (column 3, lines 15-17). It is taught that for silicone adhesives only the active substance base is suitable for use as salts thereof are practically insoluble in these types of adhesives. Additionally it is taught that if polyvinylpyrrolidone is added to the adhesive, the dissolving capacity for the free base in such matrices is increased (column 3, lines 55-67). Auxiliary substances such as alkaline substances can be added a solution of the active substance in order to convert the active substance hydrochloride into the free active substance base. Then the solution may be filtered whereby the reactants with the exception of the active substance are eliminated (column 4, lines 28-48).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al. and Muller et al. and utilize silicone adhesives. One of ordinary skill in the art would have been motivated to utilize silicone adhesives as D'Angelo et al. teach that acrylate adhesives can be utilized and Muller et al. teach that silicone adhesives or acrylate adhesives can be utilized. One of ordinary skill in the art would have been motivated to replace acrylate adhesives with silicone adhesives as both are taught by Muller et al. as functional equivalents. One of ordinary skill in the art would have a reasonable expectation of success as both D'Angelo et al. and Muller et al. are directed to transdermal delivery devices.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al. and Muller et al. and utilize rotigotine free base in the drug delivery device. One would have been motivated to add rotigotine free base to the transdermal delivery system to provide multiple unit doses of rotigotine because D'Angelo suggest that drugs used to treat Parkinson's disease may be included in the microreservoirs of the transdermal patch and Muller et al. is directed to transdermal delivery systems comprising rotigotine which is a drug taught as treating Parkinson's disease. One of ordinary skill in the art would have been motivated to utilize the rotigotine free base when utilizing silicone adhesives as it is taught by Muller et al. that the free base or the hydrochloride salt which is converted to the free base are soluble whereas salts of the active substances are practically insoluble in these types of adhesives. Furthermore, one of ordinary skill in the art would have been motivated to incorporate rotigotine into a microreservoir transdermal delivery patch as one would appreciate the desirability of administering multiple unit doses, wherein a given dose of a drug is delivered transdermally in multiple doses instead of a single large dose, as this would allow smaller doses of the drug to be administered to a patient per unit of time, which would result in less dose-related side effects.

It is noted that D'Angelo et al. teach PVP and Muller et al. teaches that if polyvinylpyrrolidone is added to the adhesive, the dissolving capacity for the free base in such matrices is increased. Therefore, one of ordinary skill in the art would have been motivated to add PVP in order to increase the dissolving capacity the drug. One of

ordinary skill in the art would have a reasonable expectation of success as D'Angelo et al. teach that PVP incorporation is suitable.

Regarding the claimed number of microreservoirs and the size of the microreservoirs, D'Angelo teaches microcapsules of a diameter of 1 to 150 microns, which vary depending on the desired concentration of the drug. Therefore, it would have been obvious to one of ordinary skill in the art to vary the number of microreservoirs or the size of the microcapsule depending on the desired amount of drug to be administered.

Regarding instant claim 10, Muller et al. teach that their invention is an improvement over WO-9407468 because WO '458 requires hydrated silicate dispersed therein for taking up the hydrophile drug salt. This results in coating products and it much more difficult to manufacture and in the system of WO '458 only the salt of the drug can be used. Muller et al. teach that their invention avoids these disadvantages (column 2, lines 5-27). Therefore, it would have been obvious to one of ordinary skill in the art to exclude silicate, which are particles that absorb salts of the amine functional drug, based on the teachings of Muller et al.

Regarding instant claims 3 and 4, as evidenced by Nugroho et al. the octanol/water distribution coefficient of rotigotine at pH 7.4 is 3.41 (page 846, last sentence) and the pKa is 7.9 (page 847, first sentence).

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. in view of Muller et al. and in further view of Quan et al. (US Patent No. 5834010, cited on PTO Form 1449).

Applicant Claims

Applicants claim the amine functional drug is oxybutynin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of D'Angelo et al. and Muller et al. are set forth above. D'Angelo et al. is directed to a multidose transdermal drug delivery system comprising microreservoirs. Pharmacological active agents taught that can administered transdermally include Parkinsonism control agents and anti-cholinergic (columns 1-2, lines 58-67 and 1-21). Muller et al. teach utilizing silicone adhesives in transdermal patches with the free base of drugs.

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

D'Angelo et al. do not teach that the anti-cholinergic drug that can be administered is oxybutynin. However, this deficiency is cured by Quan et al.

Quan et al. is directed to the use of triacetin as a penetration enhancer for transdermal delivery of a basic drug. Drugs taught that can be delivered include oxybutynin (example 1).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al., Muller et al. and Quan et al. and utilize oxybutynin as the drug to be delivered. One of ordinary skill in the art would have been motivated to utilize oxybutynin as D'Angelo et al. teach that drugs that can be delivered transdermally include anti-cholinergic drug and Quan et al. teach that oxybutynin, which is a specific anti-cholinergic, can be delivered transdermally. Furthermore, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. in view of Muller et al. and in further view of Pfister et al. (US Patent No. 5232702) and as evidenced by Nugroho et al.

Applicant Claims

Applicants claim the polymer matrix comprises two or more silicone pressure sensitive adhesives. Applicants claim the silicone pressure sensitive adhesive is a blend of a high tack silicone pressure sensitive adhesive comprising polysiloxane with a

resin and medium tack silicone pressure sensitive adhesive comprising polysiloxane with a resin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of D'Angelo et al. and Muller et al. are set forth above. D'Angelo et al. is directed to a multidose transdermal drug delivery system comprising microreservoirs. Muller et al. teach utilizing silicone adhesives in transdermal patches with the free base of drugs.

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

D'Angelo et al do not teach utilizing a blend of high tack and medium tack silicone pressure sensitive adhesives. However, this deficiency is cured by Pfister et al.

Pfister et al. is directed to silicone pressure sensitive adhesive compositions for transdermal drug delivery. Example B (column 13) teach that an adhesive formulation consisting of a low silanol containing amine compatible silicone adhesive (Adhesive II) and a high silanol containing silicone adhesive (adhesive I) were prepared. The compositions were evaluated for flow reduction and creep resistance. It is taught that adhesive II has lower cohesive strength and exhibits significantly more flow when compared to adhesive I, which in many cases this is a disadvantage where an amine compatible adhesive is required. However, by combining adhesive I and adhesive II, a significant reduction of flow and improved creep resistance was achieved.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al., Muller et al. and Pfister et al. and utilize a combination of a low silanol containing amine-compatible silicone adhesive and a high silanol containing silicone adhesive. One of ordinary skill in the art would have been motivated to utilize this combination as it is taught by Pfister et al. as providing an adhesive with significant reduction of flow and improved creep resistance where amine-compatible adhesives are required. As taught by Muller et al. when utilizing a basic drug such as rotigotine, amine-resistant adhesive are used. Therefore, one of ordinary skill in the art would have been motivated to utilize this mixture in order to provide an adhesive with significant reduction of flow and improved creep resistance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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